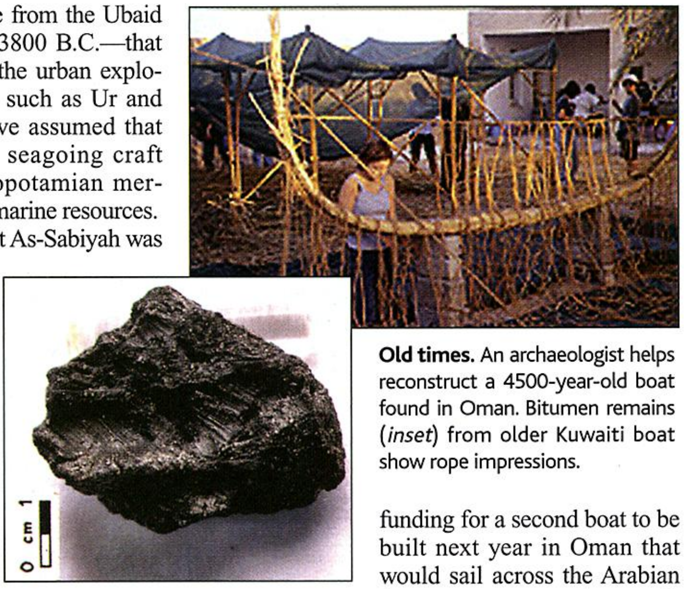
The painted shards date from the Ubaid period—6000 B.C. to 3800 B.C.—that immediately preceded the urban explosion at Sumerian sites such as Ur and Eridu. Researchers have assumed that the pottery came via seagoing craft owned by early Mesopotamian merchants eager to exploit marine resources.



Old times. An archaeologist helps reconstruct a 4500-year-old boat found in Oman. Bitumen remains (*inset*) from older Kuwaiti boat show rope impressions.

Carter speculates that As-Sabiyah was a peninsula in ancient times and an obvious first port of call for boats from the Tigris-Euphrates river system. The site likely began as a campsite and grew into a small village of stone houses whose residents might have built or repaired boats. Stone tools, coupled with the Ubaid pottery and Mesopotamian-made jewelry, hint at a mixed population of Mesopotamians and Arab Neolithic peoples, says Carter. The Arab peoples might have been nomads—similar to the Bedouin in the region today—whereas the Mesopotamians were farmers and town dwellers.

Oates maintains that Mesopotamian visitors to the Gulf region traded pottery for fish and perhaps pearls on their way south as far as Qatar and Bahrain. By the middle of the third millennium B.C., their ancestors were exchanging copper from Oman and goods from the distant Indus River valley.

The Omani find offers clues about the transport of goods back and forth across the Arabian Sea, trade that began some 3000 years after the Kuwaiti boat was built. The work, by a French-Italian team, is based on hundreds of pieces of bitumen slabs uncovered from 1985 to 1994. Led by University of Bologna archaeologist Maurizio Tosi, the team is also putting the finishing touches on a 14-meter-long vessel built of bitumen and reeds that could carry nearly 8 tons of cargo. Tosi says the boat will be ready next month, but it won't be tested in water.

The reconstruction venture earns the ire of scholars such as McGrail. McGrail says that there is not nearly enough evidence to justify such an effort. He notes that a recent reconstruction of a Viking vessel required 75% to 80% of its remains and decades of research before a realistic replica could be made. He scoffs at the Omani attempt, noting that it is not even certain the remains are from a boat. "It's crazy," he says. "It's almost wishful thinking." The boat remains provide little data on the mast, keel, rudder, and sails, adds Lamberg-Karlovsky, and the site shows no evidence of warehousing or other obvious signs of international trade. "It's a teaser," he says.

Cleuziou, who hopes to collect enough funding for a second boat to be built next year in Oman that would sail across the Arabian Sea to an area near the mouth of the Indus River in Pakistan, acknowledges that critics such as McGrail "are right to some extent." But he says that ethnographic and textual material is available to supplement the sparse archaeological evidence. For example, Sumerian writings refer to ships capable of hauling 18 tons of cargo to and from Oman. And other texts from around 2100 B.C. list specific amounts of reed bundles, rope, mats, fish oil, and bitumen to build Oman-bound ships. "Of course, this is not a proper reconstructed boat," he says, "since there are many hypotheticals."

In the absence of textual evidence for sails, for instance, the team has chosen to use reed mats instead of wool or cloth. It's also not known what types of bitumen the Sumerians used for boatbuilding. To fill the gaps, Franco D'Agostino, an archaeologist at the University of Rome, earlier this year visited a small village near Basra in southern Iraq, where bitumen is still used in boatbuilding. These methods—dying out with the draining of the marshes by the Iraqi government—have not been extensively studied.

Carter says he is also interested in trying to recreate the boat found by the British and Kuwaiti team, and he hopes to do further work next spring at As-Sabiyah. In the meantime, researchers are grateful for what appears to be the first solid evidence that boats plied the Persian Gulf as the great cities of Mesopotamia took shape, setting the stage for an international trading network. "It's damn good to have the archaeological data," says Lamberg-Karlovsky.

–ANDREW LAWLER

EVOLUTION AND DEVELOPMENT

Comparative Biology Joins The Molecular Age

Researchers are reaching ever farther down the tree of life to probe basic questions of developmental and evolutionary biology

"Too narrow," griped many biologists when in the late 1980s advocates of the Human Genome Project decided to focus sequencing efforts on just a few species. No doubt the sequences of the targeted "model" organisms—the nematode, fruit fly, mouse, human, and, later, zebrafish—would help uncover the genetic underpinnings of human disease, these researchers argued, but limiting research to this slice of the animal kingdom would leave many, more fundamental questions unanswered.

Those genome sequences couldn't explain many mysteries of development: why flies are different from sea urchins, for example, or eagles nothing like sturgeons. They would also provide few clues about evolution or the complement of genes necessary for each class of organisms. To answer such questions, "we need to sample many [places] on the tree of life," says Nipam Patel, an evo-devo researcher at the University of Chicago. Now, researchers are beginning to do just that.

Workers in dozens of labs around the world are sending new species into the sequencing pipeline. And these are not just the next six candidates—the chicken, chimp, honey bee, sea urchin, *Tetrahymena*, and fungi—the National Human Genome Research Institute (NHGRI) selected 2 weeks ago (*Science*, 31 May, p. 1589) but also species as diverse as squid, sea squirts, bats, and stickleback fish. "People are accepting the challenge of going out and [working] on organisms that are not the standard models," says Patel. As a result, the century-old science of comparative biology is making a comeback, this time with a molecular spin.

This trend was evident last month at an evo-devo meeting.* Some two dozen talks dealt with the fruit fly *Drosophila*, but dozens more tapped everything from jellyfish and the flatworm planaria to coelacanths, a living fossil fish. For researchers studying the genome sequences of humans and the original model organisms, finding

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* "Evolution of Developmental Diversity," held from 17 to 22 April at Cold Spring Harbor Laboratory, New York.

CREDITS: (TOP TO BOTTOM) THE MAGAN BOAT RECONSTRUCTION PROJECT; R. CARTER/INSTITUTE OF ARCHAEOLOGY, LONDON

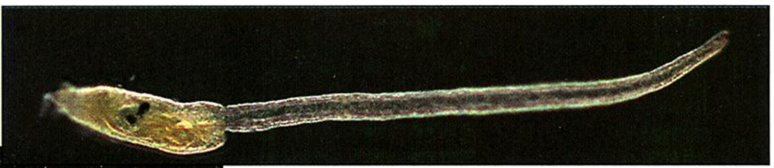
shared regions has been a key goal. That's not necessarily the case with these newcomers. "We feel the [genome sequences of] new species are interesting not only for their conserved features but also for their numerous and unexplored differences," explains Daniel Chourrout, an evo-devo researcher at the Sars International Centre for Marine Molecular Biology in Bergen, Norway.

These projects are still in their infancy, with much of the effort aimed at developing the resources needed for sequencing and for interpreting newly generated sequence data. But draft versions of a few species are either done or close to being done, and researchers are already scouring these data for new insights into how life works.

Biology's rising star

The once-understudied tunicates—simple marine organisms that live by filtering plankton—are moving toward the limelight. Their place in the history of life has made them a potential poster child for comparative molecular biology—one that might reveal how vertebrates came to be. Many researchers view tunicates as stand-ins for the evolutionary predecessor of vertebrates.

In their adult stages, most tunicates appear to have little in common with vertebrates. Sea squirts, for instance, have neither head nor tail and live attached to the sea floor. But the free-swimming sea-squirt larvae look a lot like tadpoles, with both heads and tails plus certain key features characteristic of chordates, the phylum to which both tunicates and vertebrates belong. Those features are a hollow nerve cord along the upper back, a notochord—a flexible rod of cells that functions like a backbone—and gill slits.



Vertebrates' distant kin. Although adult sea squirts look nothing like humans or fish, their embryos (*inset*) have key chordate features in common with these vertebrates, including a head, tail, dorsal nerve cord, and gill slits.

CREDITS: N. SATOH *ET AL.*/KYOTO UNIVERSITY

Only in the past decade have molecular and developmental biologists begun looking more closely at sea squirts—in particular, the species *Ciona intestinalis.* Noriyuki Satoh, a developmental biologist at Kyoto University in Japan, opted for *Ciona*, he recalls, because the body plan of its tadpole is quite sophisticated, making it useful for comparisons with the body plans of more complex vertebrates. Seven years ago he began isolating *Ciona* genes and has pulled out dozens so far, ensuring *Ciona* a place in molecular-based laboratories and making it easy for others to take on this organism.

At about the same time that Satoh began looking at the genetics of *Ciona* development, Michael Levine of the University of California (UC), Berkeley, and, independently, William Smith of UC Santa Barbara also decided to work on this species. "We believe that *Ciona* is the best model for future studies" of how development is affected by the regulation of genes, says Levine. Changes in that regulation can explain how organisms evolve to look and behave differently.

To promote *Ciona*'s utility, researchers at the Department of Energy's Joint Genome Institute in Walnut Creek, California, recently assembled a draft sequence of the 160-million-base *Ciona* genome. In April, 50 or so tunicate and bioinformatics experts joined forces to analyze the sequence, in the process discovering some 16,000 genes. Levine and Smith have also helped devise methods for introducing DNA into *Ciona*—a development that should help in determining the functions of those genes.

The researchers subject *Ciona* embryos to weak electric pulses that cause them to absorb DNA from the surrounding water. "This permits the simultaneous transformation of hundreds, even thousands of embryos," says Levine. Because the embryos have just 2600 cells, researchers can then track the effect of the inserted DNA on each cell, watching as it proliferates and specializes over time.

Using this technique, Levine and his colleagues have begun to piece together the network of genes and regulatory DNA that interact to build the *Ciona* tadpole. By surveying 200 pieces of DNA, the researchers determined the general locations of the regulatory sequences—so-called *cis*-elements—that control a gene's activity in different tissues. The elements show up about every 15,000 bases and often turn out to be very close—within 500 bases—to the gene. This proximity means that finding *cis*-elements in *Ciona* is "extraordinarily easy" compared to finding them in vertebrate genome sequences, where they are often much more distant from the genes they regulate, says Satoh. It should also make the job of determining the role *cis*-elements play in *Ciona* development easier and might even help with the identification of *cis*-elements in other organisms.

At the evo-devo meeting, Levine described his group's progress in identifying specific regulatory DNA sequences as opposed to simply determining where they reside. As a pilot test of screening the entire *Ciona* genome sequence for these elements, he and his colleagues have homed in on a 300,000-base piece of DNA that contains six so-called *Hox* genes, members of a highly conserved gene family that helps set up the body plans of organisms ranging from hydra to humans.

The researchers broke that DNA into random 3000-base pieces, added a marker gene to each one, and then inserted the hybrid DNAs one at a time into tunicate embryos. Using this approach, they found 20 regulatory elements, eight of which direct *Hox* activity. Broadening this work to the whole genome sequence, Levine plans to create "a regulatory atlas of the *Ciona* genome that could serve as a blueprint for vertebrate genomes."

Satoh is looking for genes found in mice, humans, and tunicates, but not in fruit flies or nematodes, he reported at the meeting. His survey of 10 million bases of *Ciona* DNA turned up about 30 genes that met this criterion. This result suggests that the new genome sequence can help define the genetic code for chordates. In addition, Satoh expects that many vertebrate genes will not be found among *Ciona*'s 16,000. "These [vertebrate-only] genes may help us understand what vertebrates are," he says.

Eric Lander of the Whitehead Institute Center for Genome Research in Cambridge, Massachusetts, Arend Sidow of Stanford University, and their colleagues have been sequencing *C. savignyi,* a close cousin to *C. intestinalis.* Comparisons of these two genome sequences should help pinpoint regions that underlie the speciation of these animals.

Smaller, different, better?

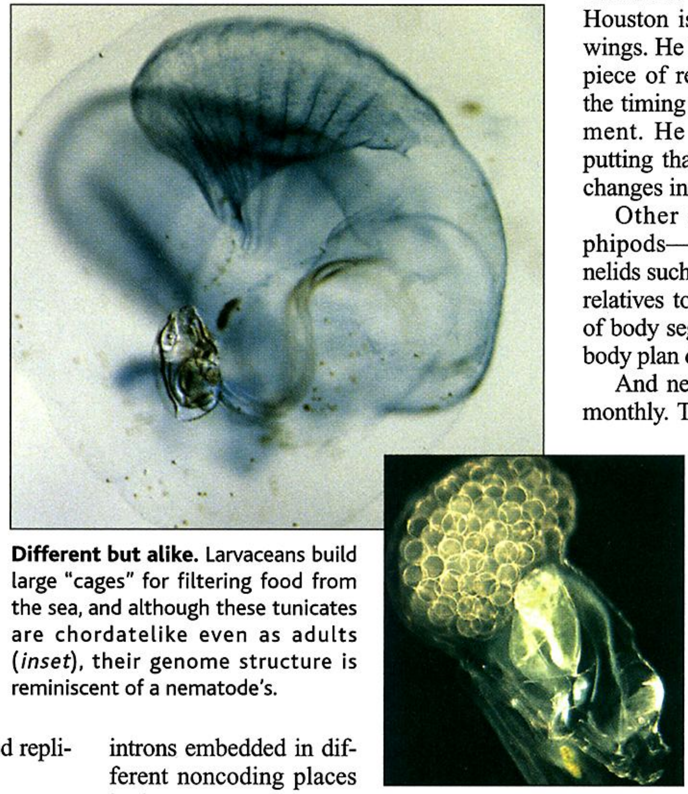
Chourrout is touting the benefits of one of *Ciona*'s more distant relatives, *Oikopleura dioica*, a so-called larvacean, for evo-devo research. In some ways the two species are quite different. Instead of being sessile, *Oikopleura* drifts along in the ocean and retains a head and tail its whole life. Thus, comparing their genome sequences should be useful. Also, because *Oikopleura* still looks like a chordate as an adult, it's relatively easy to make comparisons between it and other chordates, Chourrout notes.

Oikopleura has other advantages: It is transparent and has a small genome—only about 72 million bases compared to *Ciona*'s 160 million. It is also small and lives only 4 days, compared with *Ciona*'s 3 months. Consistent with its short life cycle, *Oikopleura* speeds through development. Its embryo takes just about 4 hours to form the notochord and less than 11 hours to develop the brain, gut, and sensory system. "It's a really nice system to work with," says Chicago's Patel.

Chourrout has teamed with Hans Lehrach of the Max Planck Institute for Molecular Genetics in Berlin to sequence *Oikopleura*'s genome. Although progress has been slow, key features have already emerged. For one, the overall organization of the *Oikopleura* genome resembles that of the nematode *Caenorhabditis elegans*, suggesting similarities in their life histories.

Both organisms have compact genomes. Chourrout reported at the meeting that *Oikopleura*'s 15,000 genes are densely packed, as are those of *C. elegans*. *Oikopleura* has one gene about every 4500 bases—compared with one gene for every 50,000 to 200,000 bases in the human genome—with far smaller noncoding DNA segments (introns) interspersed between each gene's coding regions. "The small genome may go with a short life cycle since if you have a short life cycle, you need to save a lot of time," he notes. With this genome, little time is wasted replicating noncoding DNA.

In another sign of this genomic economy, Chourrout and colleagues Hee-Chan Seo and Anne Maeland found that some of the *Hox* genes in both *C. elegans* and *Oikopleura* have lost their integrity. Ordinarily, *Hox* genes are arranged linearly in clusters, but *Oikopleura*'s *Hox* clusters "are weird," says Patel. In some places the arrangement seems skewed, and also several genes usually found in the middle are missing. He suspects that, because of its small size, *Oikopleura* might not require the organizational powers of *Hox* genes in early development the way larger, more complicated organisms do. In this regard, "*Oikopleura* is like *C. elegans*," which is also relatively small and has a simple body plan, says Chourrout.



Different but alike. Larvaceans build large "cages" for filtering food from the sea, and although these tunicates are chordatelike even as adults (*inset*), their genome structure is reminiscent of a nematode's.

CREDITS: D. CHOURROUT/SARS INTERNATIONAL CENTRE FOR MARINE MOLECULAR BIOLOGY

Other aspects of genome organization in *Oikopleura* might help protect it from genetic instability. Rolf Edvardsen, Chorrout's student at the Sars center, is studying the evolution of gene organization, focusing on how introns are arranged relative to exons, the protein-coding regions.

Edvardsen first tracked down in *Oikopleura* 11 copies of the gene coding for α-tubulin, a protein found throughout the animal kingdom that is essential for maintaining cell structure. Generally an organism's α-tubulin genes vary little, and most copies have the same introns in the same places, supposedly because this protein is so key to survival. But that's not what Edvardsen found for *Oikopleura*. Although two pairs of genes had the same intron structures, the rest had different combinations of introns embedded in different noncoding places in the gene sequence.

At the meeting Edvardsen reported "a striking difference [in intron arrangements] between *Oikopleura* and other species." In most organisms, the nature and arrangement of introns doesn't vary. Aside from other *Oikopleura* species, *C. elegans* is the only other species known to have such variability in its introns.

When introns are arranged the same way in related genes, the genes can readily swap pieces during reproduction; this swapping increases the risk that genes will become ever more similar to each other. The large difference in the intron arrangements of *Oikopleura* genes could reduce this swapping, Chourrout says.

Brave new world

Tunicates are but a few of the dozens of organisms being mined in evo-devo and genomic studies. For example, for a peek into brain evolution, Kiyokazu Agata of the RIKEN Center for Developmental Biology in Kobe, Japan, has tapped the ability of planaria to regenerate their heads. By following the formation of the new brain and characterizing the genes involved, he has early evidence that the brain organization seen in vertebrates had its beginnings in flatworms. Both vertebrate and flatworm brains have discrete regions along the anterior-posterior axis that look and function differently, and planaria's brain regions are organized like those of the embryonic vertebrate brain, he reported.

At the other end of the species spectrum, Chris Cretekos of the University of Texas M. D. Anderson Cancer Center in Houston is looking into how bats evolved wings. He has found what he thinks is a key piece of regulatory DNA that helped alter the timing and pattern of bat limb development. He hopes to demonstrate this by putting that DNA into mice and observing changes in limb development.

Other researchers have tapped amphipods—tiny, flat crustaceans—and annelids such as leeches, earthworms, and their relatives to make sense of the development of body segments. Still others are looking at body plan development in squid and hydra.

And new draft sequences are appearing monthly. The researchers who churned out the 100 million bases of the *C. elegans* genome are almost done with that of its cousin, *C. briggsae*. A second fish genome sequence, from *Fugu rubripes*—the vertebrate with the smallest genome—has been drafted and partially analyzed, as has that of a second insect, a mosquito. Sequencing of the genomes of the chimp, a sea urchin, pig, and honey bee are or are about to be under way, with more species in the wings.

To boost the comparative approach, the National Science Foundation and the National Institutes of Health have increased funding for the development of so-called BAC libraries. These sets of bacterial artificial chromosomes, which include bits of a species' entire genome sequence, make gene studies and genome sequencing easier.

The species whose genomes are now being sequenced are unlikely to achieve the status of *C. elegans* or *Drosophila* as model organisms. Nevertheless, Patel says, they are likely to contribute almost as much as these better studied counterparts toward understanding of the biological world.

–ELIZABETH PENNISI